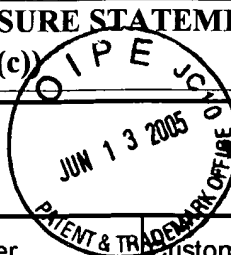


**TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT**  
(Under 37 CFR 1.97(b) or 1.97(c))

Docket No.  
16789 (PC25204A)

In Re Application Of: **David Nathan Abraham Fox, et al.**



Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/603,369	June 25, 2003	Leslie A. Royds	23389	1614	2797

Title: **NOVEL COMBINATION**

Address to:  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**37 CFR 1.97(b)**

1. ☐ The Information Disclosure Statement submitted herewith is being filed within three months of the filing of a national application other than a continued prosecution application under 37 CFR 1.53(d); within three months of the date of entry of the national stage as set forth in 37 CFR 1.491 in an international application; before the mailing of a first Office Action on the merits, or before the mailing of a first Office Action after the filing of a request for continued examination under 37 CFR 1.114.

**37 CFR 1.97(c)**

2. ☒ The Information Disclosure Statement submitted herewith is being filed after the period specified in 37 CFR 1.97(b), provided that the Information Disclosure Statement is filed before the mailing date of a Final Action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an Action that otherwise closes prosecution in the application, and is accompanied by one of:

☐ the statement specified in 37 CFR 1.97(e);

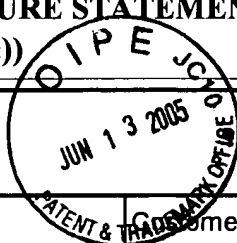
**OR**

☒ the fee set forth in 37 CFR 1.17(p).

**TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT**  
(Under 37 CFR 1.97(b) or 1.97(c))

Docket No.  
16789 (PC25204A)

In Re Application: **David Nathan Abraham Fox, et al.**



Application No.	Filing Date	Examiner	Transformer No.	Group Art Unit	Confirmation No.
10/603,369	June 25, 2003	Leslie A. Royds	23389	1614	2797

Title: **NOVEL COMBINATION**

**Payment of Fee**

(Only complete if Applicant elects to pay the fee set forth in 37 CFR 1.17(p))

- ☒ A check in the amount of **\$180.00** is attached.
- ☒ The Director is hereby authorized to charge and credit Deposit Account No. **19-1013/SSMP** as described below.
- ☐ Charge the amount of
- ☒ Credit any overpayment.
- ☒ Charge any additional fee required.
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**WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**

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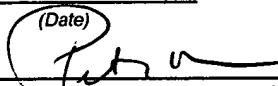
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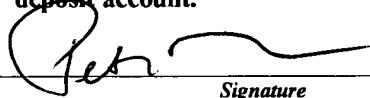
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June 9, 2005  
(Date)

  
Signature of Person Mailing Correspondence

Peter I. Bernstein  
Typed or Printed Name of Person Mailing Certificate

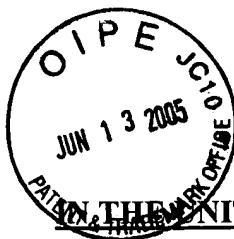
**\*This certificate may only be used if paying by deposit account.**

  
Signature

Dated: **June 9, 2005**

**Peter I. Bernstein**  
Registration No.: 43,497  
Scully, Scott, Murphy & Presser  
400 Garden City Plaza, Suite 300  
Garden City, New York 11530  
(516) 742-4343

CC:



**UNITED STATES PATENT AND TRADEMARK OFFICE**

**Applicant(s):** David Nathan Abraham Fox, et al.

**Examiner:** Leslie A. Royds

**Serial No:** 10/603,369

**Art Unit:** 1614

**Filed:** June 25, 2003

**Docket:** 16789 (PC25204A)

**For:** NOVEL COMBINATION

**Dated:** June 9, 2005

**Confirmation No.:** 2797

Mail Stop Amendment  
Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

Sir:

In accordance with 37 C.F.R. §§ 1.97 and 1.98, it is requested that the following references, which are also listed on the attached Form PTO-1449, be made of record in the above-identified case.

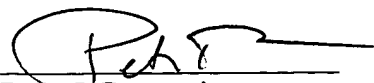
1. European Patent Publication No. EP 0 463 756 A1, published January 2, 1992;
2. European Patent Publication No. EP 0 526 004 A1, published February 3, 1993;
3. European Patent Publication No. EP 1 092 718 A1, published April 18, 2001;

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**CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: June 9, 2005

  
Peter I. Bernstein

4. European Patent Publication No. 1 092 719 A2, published April 18, 2001;
5. European Patent Publication No. 0 995 750 A1, published April 26 2000;
6. European Patent Publication No. 0 995 751 A2, published April 26, 2000;
7. PCT International Publication No. WO 91/11172, published August 8, 1991;
8. PCT International Publication No. WO 93/06104, published April 1, 1993;
9. PCT International Publication No. WO 93/07149, published April 15, 1993;
10. PCT International Publication No. WO 93/07124, published April 15, 1993;
11. PCT International Publication No. WO 93/12095, published June 24, 1993;
12. PCT International Publication No. WO 94/02518; published February 3, 1994;
13. PCT International Publication No. WO 94/05661, published March 17, 1994;
14. PCT International Publication No. WO 94/00453, published January 6, 1994;
15. PCT International Publication No. WO 95/19978, published July 27, 1995;
16. PCT International Publication No. WO 96/26940, published  
September 6, 1996;
17. PCT International Publication No. WO 98/49166, published  
November 5, 1998;
18. PCT International Publication No. WO 98/55148, published  
December 10, 1998;
19. PCT International Publication No. WO 99/54333, published  
October 28, 1999;
20. PCT International Publication No. WO 99/24433, published May 20, 1999;
21. PCT International Publication No. WO 00/24745, published May 4, 2000;
22. PCT International Publication No. WO 00/27848, published May 18, 2000;
23. PCT International Publication No. WO 01/27113 A2, published  
April 19, 2001;

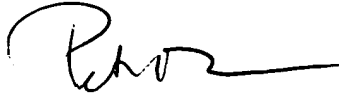
24. PCT International Publication No. WO 01/27112 A1, published April 19, 2001;
25. PCT International Publication No. WO 01/98304 A1, published December 27, 2001;
26. PCT International Publication No. WO 01/18004 A2, published March 15, 2001;
27. PCT International Publication No. WO 02/00660 A1, published January 3, 2002;
28. PCT International Publication No. WO 02/059126 A1, published August 1, 2002;
29. Fagard R.H., "Epidemiology of Hypertension in the Elderly", *The American Journal of Geriatric Cardiology*, 11(1):23-28 (2002);
30. Brown M.J. et al., "Pathoaetiology, Epidemiology and Diagnosis of Hypertension", *Drugs*, 59 suppl. 2:1-12 (2000);
31. Beevers G. et al., "The Pathophysiology of Hypertension", *BJM*, 322:912-916 (2001);
32. Ballard S.A. et al., "Effects of Sildenafil on the Relaxation of Human Corpus Cavernosum Tissue In Vitro and on the Activities of Cyclic Nucleotide Phosphodiesterase Isozymers", *The Journal of Urology*, 159:2164-2171 (1998);
33. Lipinski C.A. et al., "Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings", *Advanced Drug Delivery Reviews*, 23:3-25 (1997);
34. Stopher D. et al., "An Improved Method for the Determination of Distribution Coefficients", *Journal of Pharmacy & Pharmacology*, 42(2):144 (1990);
35. Per Artursson, et al., "Epithelial Transport of Drugs in Cell Culture II: Effect of Extracellular Calcium Concentration on the Paracellular Transport of Drugs of Different Lipophilicities Across Monolayers of Intestinal Epithelial (Caco-2) Cells", *Journal of Pharmaceutical Sciences*, 79(7):595-600 (1990);
36. Obach R.S., "The Prediction of Human Clearance from Hepatic Microsomal Metabolism Data", *Current Opinion in Drug Discovery & Development*, 4(1):36-44 (2001);

37. Shibata Y. et al., "A convenient In Vitro Screening Method For Predicting In Vivo Drug Metabolic Clearance Using Isolated Hepatocytes Suspended in Serum", *Drug Metabolism And Disposition*, 28(12):1518-1523 (2000);
38. Ward K.W. et al., "Development of an In Vivo Preclinical Screen Model to Estimate Absorption and Bioavailability of Xenobiotics", *Drug Metabolism and Disposition*, 28(1):82-88 (2001);
39. Berman J. et al., "Simultaneous Pharmacokinetic Screening of a Mixture of Compounds in the Dog Using API LC/MS/MS Analysis for Increased Throughput", *Journal of Medical Chemistry*, 40(6):827-829 (1997);
40. Han K.S. et al., "Pharmacokinetics of a Chemoprotective Agent, 2-(Allylthio) Pyrazine, After Intravenous and Oral Administration to Rats: Hepatic And Gastric First-Pass Effects", *Drug Metabolism And Disposition*, 27(2):221-226 (1999);
41. Thompson W.J. et al., "Purification and Characterization of High-Affinity Cyclic Adenosine Monophosphate Phosphodiesterase from Dog Kidney", *Biochemistry*, 18(23):5228-5237 (1979);
42. Thompson W.J. et al., "Multiple Cyclic Nucleotide Phosphodiesterase Activities from Rat Brain", *Biochemistry*, 10(2):311-316 (1971);
43. Rotella D.P. et al., "N-3-Substituted Imidazoquinazolinones: Potent and Selective PDE5 Inhibitors as Potential Agents for Treatment of Erectile Dysfunction", *J. Med. Chem.*, 43:1257-1263 (2000);
44. Pharmaprojects 4516, GlaxoSmithKline; and
45. Pharmaprojects 5051, Abbott.

Applicants are submitting copies of the above-cited references. The relevance of the above-identified references has been described in the specification.

Inasmuch as this Information Disclosure Statement is being submitted in accordance with the schedule set out in 37 C.F.R. § 1.97(c), a check in the amount of \$180.00 is enclosed.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Peter I. Bernstein", with a long horizontal flourish extending to the right.

Peter I. Bernstein  
Registration No. 43,497

Scully, Scott, Murphy & Presser  
400 Garden City Plaza, Suite 300  
Garden City, New York 11530  
(516) 742-4343

PIB/YL:kd



Form PTO-1449  
(REV. 7-80) U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

# LIST OF PRIOR ART CITED BY APPLICANT

(Use several sheets if necessary)

Atty. Docket No. (Optional)

16789 (PC25204A)

Application Number

10/603,369

Applicant(s)

David Nathan Abraham Fox, et al.

Filing Date

June 25, 2003

Group Art Unit

2797

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL*		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (if appropriate)
	AA						
	AB						
	AC						

## U.S. PATENT APPLICATION PUBLICATIONS

EXAMINER INITIAL*		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (if appropriate)
	AA						
	AB						
	AC						

## FOREIGN PATENT DOCUMENTS

	REF	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
		0 463 756 A1	1/2/92	Europe				
		0 526 004 A1	2/3/93	Europe				
		1 092 718 A1	4/18/01	Europe				
		1 092 719 A2	4/18/01	Europe				
		0 995 750 A1	4/26/00	Europe				
		0 995 751 A2	4/26/00	Europe				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Fagard R.H., "Epidemiology of Hypertension in the Elderly", <i>The American Journal of Geriatric Cardiology</i> , 11(1):23-28 (2002)
		Brown M.J. et al., "Pathoetiology, Epidemiology and Diagnosis of Hypertension", <i>Drugs</i> , 59 suppl. 2:1-12 (2000)

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



Form PTO-1449 U.S. DEPARTMENT OF COMMERCE (REV. 7-80) PATENT AND TRADEMARK OFFICE  <b>LIST OF PRIOR ART CITED BY APPLICANT</b>  <i>(Use several sheets if necessary)</i>		<b>Atty. Docket No. (Optional)</b>  16789 (PC25204A)	<b>Application Number</b>  10/603,369						
		<b>Applicant(s)</b> David Nathan Abraham Fox, et al.							
		<b>Filing Date</b> June 25, 2003	<b>Group Art Unit</b> 2797						
<b>U.S. PATENT DOCUMENTS</b>									
<b>EXAMINER INITIAL*</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>NAME</b>	<b>CLASS</b>	<b>SUBCLASS</b>	<b>FILING DATE (if appropriate)</b>		
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<b>U.S. PATENT APPLICATION PUBLICATIONS</b>									
<b>EXAMINER INITIAL*</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>NAME</b>	<b>CLASS</b>	<b>SUBCLASS</b>	<b>FILING DATE (if appropriate)</b>		
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<b>FOREIGN PATENT DOCUMENTS</b>									
	<b>REF</b>	<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>COUNTRY</b>	<b>CLASS</b>	<b>SUBCLASS</b>	<b>TRANSLATION</b>		
							<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;"><b>YES</b></td> <td style="width: 50%;"><b>NO</b></td> </tr> </table>	<b>YES</b>	<b>NO</b>
<b>YES</b>	<b>NO</b>								
		WO 91/11172	8/8/91	PCT					
		WO 93/06104	4/1/93	PCT					
		WO 93/07149	4/15/93	PCT					
		WO 93/07124	4/15/93	PCT					
		WO 93/12095	6/24/93	PCT					
		WO 94/02518	2/3/94	PCT					
		WO 94/05661	3/17/94	PCT					
		WO 94/00453	1/6/94	PCT					
<b>OTHER DOCUMENTS</b> <i>(Including Author, Title, Date, Pertinent Pages, Etc.)</i>									
		Beevers G. et al., "The Pathophysiology of Hypertension", <i>BJM</i> , 322:912-916 (2001)							
		Ballard S.A. et al., "Effects of Sildenafil on the Relaxation of Human Corpus Cavernosum Tissue In Vitro and on the Activities of Cyclic Nucleotide Phosphodiesterase Isozymers", <i>The Journal of Urology</i> , 159:2164-2171 (1998)							
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				<b>Applicant(s)</b> David Nathan Abraham Fox, et al.			
				<b>Filing Date</b> June 25, 2003		<b>Group Art Unit</b> 2797	
<b>U.S. PATENT DOCUMENTS</b>							
<b>EXAMINER INITIAL*</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>NAME</b>	<b>CLASS</b>	<b>SUBCLASS</b>	<b>FILING DATE (if appropriate)</b>
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<b>U.S. PATENT APPLICATION PUBLICATIONS</b>							
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	AA						
<b>FOREIGN PATENT DOCUMENTS</b>							
	<b>REF</b>	<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>COUNTRY</b>	<b>CLASS</b>	<b>SUBCLASS</b>	<b>TRANSLATION</b>
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		WO 95/19978	7/27/95	PCT			
		WO 96/26940	9/6/96	PCT			
		WO 98/49166	11/5/98	PCT			
		WO 98/55148	12/10/98	PCT			
		WO 99/54333	10/28/99	PCT			
		WO 99/24433	5/20/99	PCT			
		WO 00/24745	5/4/00	PCT			
		WO 00/27848	5/18/00	PCT			
		WO 01/27113 A2	4/19/01	PCT			
<b>OTHER DOCUMENTS</b> <i>(Including Author, Title, Date, Pertinent Pages, Etc.)</i>							
		Lipinski C.A. et al., "Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings", <i>Advanced Drug Delivery Reviews</i> , 23:3-25 (1997)					
		Stopher D. et al., "An Improved Method for the Determination of Distribution Coefficients", <i>Journal of Pharmacy &amp; Pharmacology</i> , 42(2):144 (1990)					
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		<b>Applicant(s)</b> David Nathan Abraham Fox, et al.	
		<b>Filing Date</b> June 25, 2003	<b>Group Art Unit</b> 2797

U.S. PATENT DOCUMENTS							
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U.S. PATENT APPLICATION PUBLICATIONS							
EXAMINER INITIAL*		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (if appropriate)
	AA						

FOREIGN PATENT DOCUMENTS								
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							YES	NO
		WO 01/27112 A1	4/19/01	PCT				
		WO 01/98304 A1	12/27/01	PCT				
		WO 01/18004 A2	3/15/01	PCT				
		WO 02/00660 A1	1/3/02	PCT				
		WO 02/059126 A1	8/1/02	PCT				

OTHER DOCUMENTS <i>(Including Author, Title, Date, Pertinent Pages, Etc.)</i>	
	Per Artursson, et al., "Epithelial Transport of Drugs in Cell Culture II: Effect of Extracellular Calcium Concentration on the Paracellular Transport of Drugs of Different Lipophilicities Across Monolayers of Intestinal Epithelial (Caco-2) Cells", <i>Journal of Pharmaceutical Sciences</i> , 79(7):595-600 (1990)
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	Shibata Y. et al., "A convenient In Vitro Screening Method For Predicting In Vivo Drug Metabolic Clearance Using Isolated Hepatocytes Suspended in Serum", <i>Drug Metabolism And Disposition</i> , 28(12):1518-1523 (2000)

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		Berman J. et al., "Simultaneous Pharmacokinetic Screening of a Mixture of Compounds in the Dog Using API LC/MS/MS Analysis for Increased Throughput", <i>Journal of Medical Chemistry</i> , 40(6):827-829 (1997)	
		Han K.S. et al., "Pharmacokinetics of a Chemoprotective Agent, 2-(Allylthio) Pyrazine, After Intravenous and Oral Administration to Rats: Hepatic And Gastric First-Pass Effects", <i>Drug Metabolism And Disposition</i> , 27(2):221-226 (1999)	
		Thompson W.J. et al., "Purification and Characterization of High-Affinity Cyclic Adenosine Monophosphate Phosphodiesterase from Dog Kidney", <i>Biochemistry</i> , 18(23):5228-5237 (1979)	
		Thompson W.J. et al., "Multiple Cyclic Nucleotide Phosphodiesterase Activities from Rat Brain", <i>Biochemistry</i> , 10(2):311-316 (1971)	
		Rotella D.P. et al., "N-3-Substituted Imidazoquinazolinones: Potent and Selective PDE5 Inhibitors as Potential Agents for Treatment of Erectile Dysfunction", <i>J. Med. Chem.</i> , 43:1257-1263 (2000)	
		Pharmaprojects 4516, GlaxoSmithKline	
		Pharmaprojects 5051, Abbott	
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